

IN THE CLAIMS

Please amend the claims as follows:

Claim 1 (Currently Amended): ~~An antagonist of a mammal prolactin receptor, wherein said antagonist is a~~

A variant of a wild-type mammalian prolactin that is an antagonist of a mammalian prolactin receptor, said variant having

the following mutations:

~~a) a mutation or set of mutations within the 14 N-terminal amino acids, wherein said mutation or set of mutations prevents the formation of the disulfide bridge between Cys<sub>4</sub> and Cys<sub>11</sub>,~~

~~a) a mutation or set of mutations within its 14 N-terminal amino acids, wherein said mutation or set of mutations prevents the formation of the disulfide bridge between the cysteine residue at position 4 and the cysteine residue at position 11, and~~

~~b) a sterically hindering mutation or set of mutations within binding site 2 of prolactin, wherein said sterically hindering mutation or set of mutations consist in the substitution of at least one residue among Ala<sub>22</sub> or Gly<sub>129</sub>, by a residue selected among Tyr, Phe, Asp, Glu, Arg, Lys and Trp;~~

wherein said wild-type mammalian prolactin has cysteine residues at position 4 and position 11 of the mature protein, an alanine residue at position 22 of the mature protein, and a glycine residue at position 129 of the mature protein.

Claim 2 (Currently Amended): [[A]] The variant of prolactin according to claim 1, wherein mutation(s) a) comprise the deletion of at least the 4 N-terminal residues of prolactin.

Claim 3 (Currently Amended): [[A]] The variant of prolactin according to claim 2, wherein mutation(s) a) comprise the deletion of the 9 N-terminal residues of prolactin.

Claim 4 (Currently Amended): [[A]] The variant of prolactin according to claim 3, having the following mutations:

a deletion of at least the 9 N-terminal residues and up to the 14 N-terminal residues; and  
a G129R substitution.

Claim 5 (Currently Amended): ~~A variant of prolactin according to any of claims 1 to 4, which is a variant of human prolactin~~

The variant of claim 1, which is a variant of human prolactin that has a human prolactin amino acid sequence except for said mutations.

Claim 6 (Currently Amended): A polynucleotide encoding the prolactin variant of claim 1 a variant of prolactin of any one of claims 1 to 5.

Claim 7 (Currently Amended): An expression cassette comprising [[a]] the polynucleotide of claim 6.

Claim 8 (Currently Amended): A recombinant vector comprising [[a]] the polynucleotide of claim 6.

Claim 9 (Currently Amended): [[An]] A host cell transformed by [[a]] the polynucleotide of claim 6.

Claim 10 (Currently Amended): A cell, organ, tissue, or transgenic non-human mammal transformed with a produced by gene transfer of, or transformation with, the polynucleotide of claim 6.

Claim 11 (Currently Amended): A therapeutic composition comprising ~~or a the~~ the polynucleotide of claim 6.

Claim 12 (Currently Amended): ~~Use of a variant of prolactin according to any of claims 1 to 5, or of a polynucleotide of claim 6 for obtaining a therapeutic composition for treating or preventing a disease involving PRL-mediated effects~~

A method for preventing or treating a disease or disorder involving PRL-mediated effects comprising administering the prolactin variant of claim 1 to a subject in need thereof in an amount sufficient to antagonize the activity of prolactin.

Claim 13 (New): A variant of a mammalian prolactin which has the following mutations compared to the corresponding wild-type mammalian prolactin:

- a) one or more mutations within the 14 N-terminal amino acids of the corresponding mature wild-type prolactin which prevent the formation of a disulfide bridge between the cysteine residues corresponding to positions 4 and 11 of the mature wild-type prolactin, and
- b) at least one sterically hindering substitutional mutation at Ala<sub>22</sub> or Gly<sub>129</sub>, or both, of the sequence of binding site 2 of the corresponding wild-type mammalian prolactin; wherein the mature wild-type mammalian prolactin has cysteine residues at positions 4 and 11, an alanine residue at position 22, and a glycine residue at position 129.

Claim 14 (New): The variant of claim 13, which contains a deletion of at least one of the cysteine residues at positions 4 or 11 of the corresponding mature wild-type prolactin.

Claim 15 (New): The variant of claim 13, which contains a substitution of a non-cysteine amino acid residue for at least one of the cysteine residues at positions 4 or 11 of the corresponding mature wild-type prolactin.

Claim 16 (New): The variant of claim 13, which contains a deletion of 9 to 14 N-terminal amino acid residues of the mature wild-type prolactin.

Claim 17 (New): The variant of claim 13, which contains a deletion of 9 to 14 N-terminal amino acid residues of the mature wild-type prolactin and a substitution with arginine of the glycine residue corresponding to position 129 of the mature wild-type prolactin.

Claim 18 (New): The variant of claim 13, in which the agonist activity of the prolactin variant on the prolactin receptor is abolished or reduced compared to the corresponding mature wild-type prolactin molecule.

Claim 19 (New): The variant of claim 13, which is a variant of human prolactin that has a human prolactin amino acid sequence except for said mutations.

Claim 20 (New): A method for treating a disease or disorder mediated by prolactin comprising administering the prolactin variant of claim 13 to a subject in need thereof in an amount sufficient to antagonize the activity of prolactin.